Study Title:	THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI) NCT06110572
Version Date:	16MAY2023
PI:	Evan Osmundson, MD PhD

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:

Small-cell lung cancer (SCLC) is an aggressive form of lung cancer with associated high morbidity and mortality that affects ~30,000 people per year in the United States. Treatment for limited stage (LS-SCLC) disease involves treatment with concurrent chemotherapy and radiation to the chest, as well as prophylactic cranial irradiation (PCI). Extensive stage disease (ES-SCLC) has historically been treated with chemotherapy alone with consideration of consolidative thoracic radiotherapy for those with response to chemotherapy, as well as consideration of addition of PCI. Emerging pre-clinical and clinical evidence supports the synergistic interactions between immunotherapy and radiotherapy.

This study will evaluate a novel radiotherapy regimen of low dose total body irradiation (LD-TBI) and hypo-fractionated RT (H-RT) in the induction therapy phase for ES-SCLC in combination with standard of care atezolizumab plus platinum doublet chemotherapy to enhance anti-tumoral immune responses. Patients will undergo treatment with LD-TBI (0.1 Gy x 2, BID) given 2-3 days prior to start of cycle 2 (first dose of atezolizumab). This will be followed by H-RT (8 Gy x 3) to all measurable sites of disease (up to 10). An additional 8 Gy x 3 will be delivered to residual sites of disease following induction systemic therapy.

The target enrollment is 18 patients. This study seeks to add total body irradiation (TBI) and hypo-fractionated radiotherapy (H-RT) to involved sites to standard of care chemo-immunotherapy for patients with ES-SCLC. We assume a 24-month accrual period with at least 6 months of follow-up on every patient.

Study Title: THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date: 16MAY2023
PI: Evan Osmundson, MD PhD

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you have small cell lung cancer (SCLC) that has spread to disease sites outside of the lung (extensive stage) and your doctor is recommending the following treatment: low dose of radiation to the whole body, along with high dose radiation to all sites of cancer observed on imaging, combined with chemotherapy and immune therapy.
The purpose of this study is to investigate whether combining low dose radiation to the entire body plus higher dose radiation to known areas of cancer with standard of care chemotherapy and immune therapy will improve response to treatment.

You will be asked to undergo a total of two radiation treatments to the whole body, followed by three additional radiation treatments to sites of known cancer detected on imaging. Furthermore, an additional three radiation treatments may be delivered after additional chemotherapy and immune therapy based on response to treatment.

The addition of total body and focused radiation to standard of care chemotherapy and immunotherapy is investigational. This means the treatment as performed in this study has not been approved as a standard treatment by regulatory health authorities, such as the U.S. Food and Drug Administration (FDA).

The addition of radiation treatment may improve disease control; however, it may contribute to increased treatment associated side effects.

If you choose not to participate in this study, you would typically be treated with guideline recommend chemotherapy and immune therapy alone.

In this study, we hope to determine how adding low dose total body irradiation and higher dose tumor-directed radiation to standard of care chemotherapy and immunotherapy can improve disease control and patient outcomes.

Study Title:	THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date:	16MAY2023
PI:	Evan Osmundson, MD PhD

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:
The combination of radiation with chemotherapy and immunotherapy as performed in this study has not been previously tested, and thus may be associated with increased treatment side effects.

Radiation combined with immunotherapy has been demonstrated to be generally safe based on previous studies, however, unexpected severe side effects could arise using this new approach. The side effects and risks will be based on the site of the body that is being treated with radiation therapy.

Expected side effects of radiation could include, but are not limited to:

- Pneumonitis (inflammation of the lung)
- Esophagitis (irritation of the esophagus between the mouth and stomach)
- Fatigue
- Pain
- Injury to bowel (small or large intestine), spinal cord, kidney, or other organs.

Chemotherapy has known side effects including, but not limited to:

- Reduced blood cell counts (increased risk of infection or bleeding; can cause fatigue)
- Mucositis (inflammation of tissue lining organs such as the mouth, throat, esophagus, stomach, and bowel)
- Esophagitis (irritation of the esophagus between the mouth and stomach)
- Fatigue.

Additionally, immunotherapy has known side effects including, but not limited to:

- Pneumonitis (inflammation of the lung)
- Thyroiditis (thyroid dysfunction)
- Colitis (inflammation of the bowel)
- Pericardial disorders (inflammation of pericardium)

Study Title:	THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date:	16MAY2023
PI:	Evan Osmundson, MD PhD

Radiation Risks: This research study may involve exposure to radiation from 2 CT Head Scans. This radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation that you will receive by participating in this study is equal to your body receiving 11 months of radiation from your natural surroundings, or about 5.7% of the amount allowed in a year for people who are exposed to radiation as part of their work.

Radiation doses will be guided by acceptable national parameters of safe delivery doses thus we anticipate a minimal additional clinical risk of side effects from this treatment regimen.

Risks that are not known:
Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

Good effects that might result from this study:
The benefits to science and humankind that might result from this study:

- demonstrating the efficacy of addition of low dose total body irradiation and higher dose tumor directed radiation to standard chemotherapy and immunotherapy in patients with extensive stage small cell lung cancer.
- Improving your chance for cancer control and clinical outcome.

Procedures to be followed:
You will undergo additional testing, imaging and follow-up before, during and after treatment on this study detailed in schedule of events for study.

Screening
You will have the following done within 21 days prior to enrolling in the study, in order to determine if you are a good candidate for the study:

- Review of your general medical history including information about your disease and what previous treatments you may have received.
- You will be asked about your level of activity.
- Physical exam that includes obtaining your body weight, height, and vital signs (blood pressure, heart rate, breathing rate, oxygen saturation, and temperature).
- You will be asked about and you should tell your study doctor about any problems you are having and the medicines you are taking, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Study Title: THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date: 16MAY2023
PI: Evan Osmundson, MD PhD

- Collection of about ¾ tablespoon of blood for routine laboratory testing (including blood counts and blood chemistry, PT/PTT, TSH level to check your heart, thyroid levels, and ability of your blood to clot); and also blood testing for HIV (AIDS), Hepatitis B and Hepatitis C.
- Urine test to check your kidney function and overall health (about ¼ cup of urine).
- If you are a woman capable of becoming pregnant, you will have either a urine or blood pregnancy test.
- Computed tomography (CT) or magnetic resonance imaging (MRI) performed within 8 weeks prior to your first dose of study drug will be reviewed to check the current state of your disease. This scanning may be part of your standard of care. If your most recent available scans were performed more than 8 weeks before you start treatment in this study, repeat scanning may need to be done just for this study and not as standard of care.
- Obtainment of diagnostic tumor tissue (archival or new biopsy/resection) for biomarker testing.

Day 1 (Week 1 / Cycle 1, Day 1)
If you are eligible for the study, you will return to clinic to start the study treatment; the following things will be done:

- Physical exam and laboratory tests (unless already completed during screening ≤ 7 days prior to starting Day 1 study treatment):
  - Physical exam, body weight, and questions about your level of activity.
  - Collection of about ½ tablespoon of your blood for routine laboratory testing (including blood counts and blood chemistry, troponin level to check your heart, and thyroid hormone levels).
  - If you are a woman capable of becoming pregnant, you will have either a urine or blood pregnancy test.
- Questions about any side effects that you are experiencing and any changes to your medications.
- Vital signs
- **Carboplatin/Etoposide/Atezolizumab**: intravenous (IV) infusion into a vein

Day 2 and 3 (Cycle 1, Day 2 and Cycle 1, Day 3)

- **Etoposide**: intravenous (IV) infusion into a vein
- Questions about any side effects that you are experiencing and any changes to your medications.

Day 18 or 19 (Cycle 1, Day 18 or 19)

Study Title: THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date: 16MAY2023
PI: Evan Osmundson, MD PhD

- Collection of about ½ tablespoon of your blood for routine laboratory testing (including blood counts and blood chemistry, troponin level to check your heart, and thyroid hormone levels).
- Questions about any side effects that you are experiencing and any changes to your medications.
- Vital signs
- TBI- a total dose of 0.2 Gy in 0.1 Gy fractions given twice daily will be delivered per institutional protocol.

Cycle 2, Day 1

- Physical exam and laboratory tests
  - Physical exam, body weight, and questions about your level of activity.
  - Collection of about ½ tablespoon of your blood for routine laboratory testing (including blood counts and blood chemistry, troponin level to check your heart, and thyroid hormone levels).
  - If you are a woman capable of becoming pregnant, you will have either a urine or blood pregnancy test.
- Questions about any side effects that you are experiencing and any changes to your medications.
- Vital signs
- **Carboplatin/Etoposide/Atezolizumab**: intravenous (IV) infusion into a vein
- Hypofractionated RT (Continued on Cycle 2, Day 2 and Day 3) - 8 Gy x 3 will be delivered to all sites of radiologically apparent gross disease (up to 10 metastatic sites, and thoracic primary) over the course of 7 calendar days, although treatment of metastatic sites over consecutive days is highly encouraged. The first of the three 8 Gy fractions must be delivered on TBI +2-3 days

Cycle 2, Day 2 and Day 3 (Same for Cycle 3, Day 2 and 3 and Cycle 4, Day 2 and 3)

- **Etoposide**: intravenous (IV) infusion into a vein
- Questions about any side effects that you are experiencing and any changes to your medications.

Cycle 3, Day 1 and Cycle 4, Day 1

- Physical exam and laboratory tests):
  - Physical exam, body weight, and questions about your level of activity.

Study Title: THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date: 16MAY2023
PI: Evan Osmundson, MD PhD

  - Collection of about ½ tablespoon of your blood for routine laboratory testing (including blood counts and blood chemistry, troponin level to check your heart, and thyroid hormone levels).
  - If you are a woman capable of becoming pregnant, you will have either a urine or blood pregnancy test.
- Questions about any side effects that you are experiencing and any changes to your medications.
- Vital signs
- **Carboplatin/Etoposide/Atezolizumab**: intravenous (IV) infusion into a vein

Cycle 3, Day 15

- Computed tomography (CT) or magnetic resonance imaging (MRI) to check your disease. Tumor response assessment with CT C/A/P at 8 weeks post C1D1, 4 weeks post last cycle of chemoimmunotherapy (+28d from cycle 4 or 6) and then q2-3 months during 1st year; MRI brain at 4 weeks post last cycle of chemoimmunotherapy then q3-4 months during 1st year.

Cycle 5, Day 1 (every additional cycle)- **Maintenance Phase**

- Physical exam and laboratory tests (unless already completed during screening ≤ 7 days prior to starting Day 1 study treatment):
  - Physical exam, body weight, and questions about your level of activity.
  - Collection of about ½ tablespoon of your blood for routine laboratory testing (including blood counts and blood chemistry, troponin level to check your heart, and thyroid hormone levels).
  - If you are a woman capable of becoming pregnant, you will have either a urine or blood pregnancy test.
- Questions about any side effects that you are experiencing and any changes to your medications.
- Vital signs
- **Atezolizumab**: intravenous (IV) infusion
- Computed tomography (CT) or magnetic resonance imaging (MRI) to check your disease. Tumor response assessment with CT C/A/P at 8 weeks post C1D1, 4 weeks post last cycle of chemoimmunotherapy (+28d from cycle 4 or 6) and then q2-3 months during 1st year; MRI brain at 4 weeks post last cycle of chemoimmunotherapy then q3-4 months during 1st year.

Study Title:	THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date:	16MAY2023
PI:	Evan Osmundson, MD PhD

30-Day Follow-Up:
30 days after your final treatment in this study, you have the following things done as part of follow-up:

- Physical exam.
- Questions about your level of activity, any side effects that you are experiencing and any changes to your medications.
- Collection of about ¼ tablespoon of your blood for routine laboratory testing (including blood counts and blood chemistry, and troponin level to check your heart).

Follow-Up

- Each patient will be followed for survival and information about subsequent anticancer therapy every 3-4 months ±14 days after patient's final protocol treatment with carbo/etop/atezo (whichever occurs last), until death, termination of the study, patient withdraws consent, or for a maximum of 3 year(s) after the patient's final protocol-indicated treatment – whichever comes first. Contact can be made via clinic visit, chart review, obituary or similar observation (e.g. Social Security death index), or by telephone.

Payments for your time spent taking part in this study or expenses:
You will not be compensated for taking part in this study.

Costs to you if you take part in this study:
If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Study Title:	THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date:	16MAY2023
PI:	Evan Osmundson, MD PhD

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator that an injury occurred, then you and/or your insurance may be billed for the cost of medical care provided at Vanderbilt to treat the injury. You will be responsible for any copayments or deductibles associated with the treatment of that injury.

There are no plans for Vanderbilt to pay for the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact [redacted]

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the [redacted]

Reasons why the study doctor may take you out of this study:
Primary reason will be if there is an inability to establish proper follow-up with you or for some reason you are unable to complete standard of care treatment.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry:
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Confidentiality:
Records and data collected in this study will be maintained in your Vanderbilt University Medical Center patient chart accessible by the medical staff that performed direct medical care for you. Data analyzed in this clinical trial will be stored in a secure online database and accessed by secure computers on the Vanderbilt network.

Study Title: THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI) NCT06110572
Version Date: 16MAY2023
PI: Evan Osmundson, MD

Vanderbilt may share your information, without identifiers, to others or use if for other research projects not listed in this form. Vanderbilt, Dr. Evan Osmundson, and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

This study is supported by funding from Varian Medical. Sharing of information generated from this study with the sponsor will be governed by applicable policies from Vanderbilt University Medical Center and agreements between Vanderbilt and the sponsor.

Information that must be reported by law, such as child abuse or some infectious diseases, is not protected under this confidentiality agreement. This agreement does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Study Results:
Records and data collected in this study will be maintained in your Vanderbilt University Medical Center patient chart accessible by the medical staff that performed direct medical care for you. Data analyzed in this clinical trial will be stored in a secure online database and accessed by secure computers on the Vanderbilt network.

Vanderbilt may share your information, without identifiers, to others or use if for other research projects not listed in this form. Vanderbilt, Dr. Evan Osmundson, and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

Study Title:	THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date:	16MAY2023
PI:	Evan Osmundson, MD PhD

Authorization to Use/Disclose Protected Health Information

What information is being collected, used, or shared?

To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?

The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?

You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?

Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?

You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

Study Title: THOP2206 TESSERACT: Trial in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) to Enhance Response to Atezolizumab and Chemotherapy with Total Body Irradiation (TBI)
Version Date: 16MAY2023
PI: Evan Osmundson, MD PhD

You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds this data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

_____ _____
Date Signature of patient/volunteer

Consent obtained by:

_____ _____
Date Signature

_____
Printed Name and Title

Time: _____